Amendments to the Drawings:

The attached sheets of drawings are black and white versions of the previously submitted drawings, which included several drawings in color, but are otherwise identical to the original drawings. These sheets, which include Figures 1-25, replace the original sheets containing Figures 1-25.

Attachment: Replacement Sheets (16)

REMARKS

Claims 52, 53 and 55-81 were pending in the present application and claims 55-70 were withdrawn from consideration. The PTO acknowledges that the subject matter of claim 81 is allowable if that claim were rewritten in independent form, such that claim 81 is merely objected-to whilst claims 52, 53 and 55-80 stand finally rejected. By the amendment submitted herewith, claims 55-70 are canceled without prejudice to the prosecution of the encompassed subject matter in any related continuation, continuation-in-part or divisional application, and claims 52, 77-79 and 80 are amended to more particularly point out and distinctly claim certain embodiments encompassed by the invention.

Support for the present amendments may be found in the application as originally filed, for example, in the specification as published at paragraphs 0102, 0108, 0140, 0141, 0237-0243 and elsewhere. No new matter is introduced by way of the present amendment.

DRAWINGS

The PTO objects to the Drawings, asserting that they include drawings in color and that no petition under 35 C.F. R. 1.84(b)(2) has been submitted. Presented herewith for approval are 16 replacement sheets of drawings containing Figures 1-25, which have been amended solely to reflect correction of the Drawings to no longer include color drawings. Withdrawal of this objection is therefore respectfully requested.

ELECTION/ RESTRICTIONS

The PTO asserts that a complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action, noting Applicants' previous traversal.

Solely for purposes of moving the application forward to allowance and without acquiescence in view of the Final Office Action, claims 55-70 are canceled without prejudice by the amendment submitted herewith. It is submitted that the application has been placed in condition for allowance by the present amendment.

REJECTIONS UNDER 35 U.S.C. 112, SECOND PARAGRAPH

The PTO rejects claims 52, 53 and 71-80 for alleged indefiniteness. More specifically, the Examiner is unclear as to the meaning of the phrase "% sequence similarity" and notes in the Action at page 4, lines 1-2 that this rejection could be obviated if the claims referred to sequence identity rather than sequence similarity.

Applicants traverse these grounds for rejection and submit that the meaning of the claims is clear. As recited by the claims and disclosed in the specification, for example, at paragraph 0141 of the published application, the meaning of % sequence "similarity" is clear and would be understood by the person having skill in the art.

Nevertheless, solely for purposes of advancing the prosecution of the application by removing issues of record in the final rejection, and without acquiescence in the rejection, claims 52 and 77-80 as amended herewith recite "% sequence identity" as recommended by the Examiner to obviate the indefiniteness rejection.

Accordingly it is respectfully requested that upon entry of the amendment submitted herewith, the indefiniteness rejection will be reconsidered and withdrawn.

REJECTIONS UNDER 35 U.S.C. 112, FIRST PARAGRAPH

The PTO rejects claims 52, 53 and 71-80 for allegedly failing to meet the written description requirement. In particular, the Examiner asserts that the specification and claims discuss "substantial homology" only in relation to the full length sequences of SEQ ID NOS:19-21 and not to the 350-390 fragment of SEQ ID NO:21. The Examiner alleges further that for the claims to encompass an agent that comprises a polypeptide having an amino acid sequence that exhibits less than 100% sequence identity to amino acids 350 to 390 of SEQ ID NO: 21 impermissibly constitutes added matter.

Applicants respectfully traverse these grounds for rejection. The present embodiments are directed in pertinent part to a method for controlling entry of a flavivirus into a cell, the flavivirus exhibiting a flavivirus envelope protein, the flavivirus envelope protein comprising a domain III of the flavivirus envelope protein, the method comprising administering to the cell an agent that functionally interferes with binding of the domain III of the flavivirus

envelope protein to a flavivirus receptor protein, wherein the agent comprises a polypeptide having an amino acid sequence that exhibits at least 80% sequence identity to amino acids 350 to 390 of a flavivirus envelope sequence as set forth in SEQ ID NO: 21, and wherein the flavivirus receptor protein is one of an integrin and a neurotensin receptor.

As a first matter, Applicants thank the Examiner for acknowledging that the subject matter of claim 81 is allowable, where claim 81 relates to the above recited method wherein the agent comprises a polypeptide having an amino acid sequence that exhibits complete identity to amino acids 350 to 390 of a flavivirus envelope sequence as set forth in SEQ ID NO: 21. In particular, and for reasons also previously made of record, the instant specification teaches that amino acids 350 to 390 functionally interfere with binding of domain III of a flavivirus envelope protein to a flavivirus receptor protein that is an integrin or neurotensin receptor (*e.g.,* paragraphs 0237-0243).

In traversal of the present rejection, Applicants note that the skilled person would understand that the instant specification, for example at paragraph 0102, teaches that competitive ligands, such as the presently recited agent that functionally interferes with binding of the domain III of the flavivirus envelope protein to a flavivirus receptor protein, can include a peptide that is complementary to the binding region in the integrin or neurotensin receptor. As disclosed therein, such a peptide can be identified by the person of skill in the art based on "information" provided in the specification. Information in the specification includes, for example, the disclosure at paragraph 0108, that preferably the domain III of the flavivirus envelope protein comprises a *portion* having a sequence *substantially homologous* to SEQ ID NO:21 (emphasis added).

It is therefore emphasized in this regard that a portion would be understood by the skilled person to be less than a full length polypeptide (*e.g.,* 350-390), as appreciated by the PTO, but that contrary to the assertion found in the Action, a substantially homologous portion would be readily understood by such skilled person as one that exhibits less than 100% sequence identity (*e.g.*, to amino acids 350 to 390 of SEQ ID NO: 21).

At paragraph 0140 of the specification, for example, there is provided the teaching that a "polypeptide" and a "protein" are <u>not</u> to be limited by having a minimum polymer

length, but instead encompass full-length proteins and fragments thereof. Such fragments clearly may include amino acids 350 to 390 of SEQ ID NO:21, as Applicants have previously noted and as the PTO readily concedes in the Action at page 5.

Furthermore, however, it is submitted that the PTO fails to consider the final sentence of paragraph 0140 in the published application. Therein it is disclosed expressly that "the term 'polypeptide' refers also to a modified protein including protein comprising deliberate or accidental modifications of the original sequence, such as *deletions, additions and substitutions*, so long as the protein maintains the desired activity" (emphasis added).

The skilled person would therefore clearly understand from paragraph 0140 that the presently recited agent may be a polypeptide having the amino acid sequence of amino acids 350 to 390 of SEQ ID NO:21 *or* a "modified protein including protein comprising deliberate or accidental modifications of the original sequence, such as deletions, additions and substitutions, so long as the protein maintains the desired activity" *i.e.,* functionally interfering with binding of the domain III of the flavivirus envelope protein to a flavivirus receptor protein that is an integrin or a neurotensin receptor.

Moreover, in the context of the instant claims it is submitted that the skilled person would understand from the disclosure in the very next paragraph in the specification, paragraph 0141, that the recited agent encompasses a "substantially homologous" polypeptide that includes any *structurally* similar polypeptide ranging from one having at least 80% sequence similarity to one showing complete identity to SEQ ID NO:21 and that, as recited in the present claims, maintains the desired activity, *i.e., functionally* interferes with binding of the domain III of the flavivirus envelope protein to the flavivirus receptor protein.

Accordingly, it is submitted that the specification at, *e.g.,* paragraph 0140 clearly contemplates a fragment of a polypeptide such as amino acids 350 to 390 of SEQ ID NO:21, and further clearly contemplates a modified polypeptide such as one having deletions, additions and substitutions, so long as the protein maintains the desired activity. It is submitted further that the specification at, *e.g.,* paragraph 0108 (cited *supra*) clearly contemplates that a "portion" of a domain III polypeptide may have a sequence that is "substantially homologous" to SEQ ID NO:21, where 80-85%, 90% and 95-98% sequence identity are all clearly encompassed within

"substantially homologous" according to paragraph 0141, and that paragraph 0102 (cited *supra*) also clearly contemplates such competitive ligands of domain III-integrin (or domain III-neurotensin receptor) binding interactions.

It is therefore submitted that a person skilled in the art would understand the instant specification as disclosing not only an agent that comprises a polypeptide having an amino acid sequence that exhibits complete identity to amino acids 350 to 390 of a flavivirus envelope sequence as set forth in SEQ ID NO: 21, as has already been conceded by the PTO (claim 81), but as also disclosing that such an agent may include a modified sequence having at least 80%, 85%, 90%, 95% or greater sequence identity to amino acids 350 to 390 of SEQ ID NO:21. As such, no new matter has been added and the application complies with the requirements of 35 U.S.C. 112, first paragraph.

In view of the foregoing, reconsideration and withdrawal of the rejections are respectfully requested.

Applicants believe that upon entry of the amendment submitted herewith, the application will be in condition for allowance. Should the PTO believe that there remain any unresolved issues in the application, the Examiner is urged to contact the Applicants' undersigned representative by telephone to discuss the same.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

/Stephen J. Rosenman/
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SJR:rp

Enclosures:
16 Sheet(s) of Drawings (Figures. 1-25)

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